

b.) Amendments to the Specification

Please insert the following new paragraph on page 1 after line 1, before line 2.

This application is a division of U.S. Application No. 09/791,602 filed February 26, 2001, which in turn is a division of U.S. Application No. 09/513,472 filed February 25, 2000 (now U.S. Patent No. 6,239,168), which in turn is a division of U.S. Application No. 09/091,752 filed June 24, 1998 (now U.S. Patent No. 6,316,491) which in turn is a 371 of PCT/JP97/03874.

Please amend the paragraph starting at page 41, line 7 and ending at page 42, line 4 to read as follows.

The cells were inoculated into a 96 well microplate (# 167008, *manufactured* by Nunc) in an amount of 1,000 cells per well and pre-cultured at 37°C for 24 hours in a 5% carbon dioxide gas incubator using Dulbecco's modified Eagle's medium (DMEM) which had been supplemented with 10% fetal calf serum (FCS). Next, a DMSO solution of each test compound which had been adjusted to 10 mM was serially diluted with the culturing medium and added to the wells in 50 $\text{m}\mu\text{l}$ portions. Thereafter, the culturing was continued at 37°C for 72 hours in the 5% carbon dioxide gas incubator. Five hours before completion of the culturing, 3-(4,5-dimethylthiazo-2-yl)-2,5-diphenyltetrazolium bromide (manufactured by Sigma, hereinafter referred to as "MTT") which had been dissolved in the culturing medium to a final concentration of 1 mg/ml $\text{mg}/\mu\text{l}$ was dispensed into the wells in 50 $\text{m}\mu\text{l}$ portions. After completion of the culturing, DMSO was dispensed into the wells in 150 ml portions, and the plate was vigorously stirred using a plate mixer to dissolve MTT-formazan crystals completely. Thereafter, absorbance at 550 nM μl was measured using a microplate reader MTP-32 (manufactured

by Corona Denki). The cell growth inhibition activity was expressed by 50% inhibition concentration (IC_{50}).

Please amend the paragraph at page 59, lines 2-10 to read as follows.

Major component: 1H -NMR ($CDCl_3$) δ (ppm): 10.78 (1H, br), 7.86 (1H, br s), 7.14 (1H, dd, 15.8, 11.6Hz), 6.75 (1H, d, 15.8Hz), 6.60 (1H, s), 6.09 (1H, dd, 11.6, 10.2Hz), 5.60 (1H, dd, 10.6, 3.0Hz), 5.47 (1H, m), 4.85 (1H, d, 13.9Hz), 4.79 (1H, d, 13.9Hz), 4.69 (1H, br), 3.98 (1H, br), 3.37 - 3.56 (4H, m), 3.16 (1H, br), 2.94 (2H, dd, 8.6, 2.6, 2.3Hz), 2.31 (1H, ddd, 15.2, 3.6, 3.6Hz), 1.95 (1H, ddd, 15.2, ~~4.0~~ 8.9, 4.0Hz), 1.74 (2H, br), 1.53 (3H, d, 6.9Hz), 1.49 - 1.58 (2H, br), 1.20 - 1.29 (4H, br).

Please amend the paragraph at page 59, lines 15-22 to read as follows.

Major component: 1H -NMR ($CDCl_3$) δ (ppm): 10.99 (1H, br), 8.00 (1H, br), 7.16 (1H, m), 6.73 (1H, d, 16.2Hz), 6.59 (1H, s), 6.11 (1H, dd, 10.6, 10.2Hz), 5.62 (1H, br d, 9.6Hz), 5.48 (1H, m), 4.80 (2H, s), 4.67 (1H, d, 12.2Hz), 4.54 (2H, br), 4.00 (1H, br), 3.73 - 3.89 (2H, br), 3.17 (1H, br), 3.04 (1H, m), 2.50 - 2.65 (2H, m), 2.32 (1H, ddd, 15.2, 3.6, 3.3Hz), 1.93 (1H, ddd, 18.8, ~~4.6~~ 9.2, 4.6Hz), 1.58 - 1.70 (2H, m), 1.54 (3H, d, 6.9Hz), 1.04 - 1.19 (2H, m), 0.94 (3H, d, 6.3Hz).

Please amend the paragraph at page 62, lines 17-24 to read as follows.

Major component: 1H -NMR ($CDCl_3$) δ (ppm): 10.76 (1H, br), 7.23 (1H, dd, 15.5, 10.9Hz), 6.84 (1H, br), 6.69 (1H, d, 16.2Hz), 6.67 (1H, br), 6.16 (1H, dd, 11.2, 10.6Hz), 5.70 (1H, dd, 10.4, 3.1Hz), 5.51 (1H, m), 4.75 (1H, br), 4.64 (2H, s), 4.10 (1H, br), 3.45 - 3.57 (6H, m), 3.22 (1H, br), 2.99 (1H, ddd, 8.3, 2.6, 2.3Hz), 2.36 (1H, ddd, 15.2, 3.6, 3.3Hz), 2.00 (1H, ddd, 15.2, ~~4.3~~ 8.6, 4.0Hz), 1.58 (3H, d, 6.6Hz), 1.14 (3H, t, 7.1Hz).

Please amend the paragraph at page 63, lines 5-12 to read as follows.

Major component: $^1\text{H-NMR}$ (CDCl_3) δ (ppm): 10.77 (1H, br), 7.47 (1H, br), 7.24 (1H, dd, 16.1, 11.2Hz), 6.68 (1H, d, 16.2Hz), 6.61 (1H, s), 6.40 (1H, br), 6.16 (1H, dd, 11.6, 11.5Hz), 5.86 (1H, m), 5.70 (1H, dd, 10.2, 3.3Hz), 5.51 (1H, m), 5.23 (1H, dd, 17.2, 1.3Hz), 5.16 (1H, dd, 10.2, 1.3Hz), 4.71 (1H, br), 4.64 (2H, s), 3.96 - 3.98 (3H, m), 3.21 (1H, br), 2.99 (1H, m), 2.35 (1H, ddd, 15.2, 3.6, 3.3Hz), 1.98 (1H, ddd, 15.2, 4.0 8.9, 4.0Hz), 1.56 (3H, d, 6.9Hz).

Please amend the paragraph at page 64, lines 5-13 to read as follows.

Major component: $^1\text{H-NMR}$ (CDCl_3) δ (ppm): 10.71 (1H, br), 7.75 (1H, br), 7.20 (1H, dd, 16.0, 11.4Hz), 6.64 (1H, d, 15.8Hz), 6.54 (1H, s), 6.52 - 6.64 (3H, m), 6.11 (1H, dd, 11.5, 10.2Hz), 5.67 (1H, dd, 10.2, 3.3Hz), 5.46 (1H, m), 4.69 (1H, d, 13.5Hz), 4.63 (1H, d, 16.2Hz), 4.62 (1H, br), 4.45 (1H, d, 5.9Hz), 3.99 (1H, d, 15.8Hz), 3.83 (3H, s), 3.82 (3H, s), 3.81 (3H, s), 3.18 (1H, br), 2.96 (1H, m), 2.33 (1H, ddd, 15.2, 3.6, 3.6Hz), 1.95 (1H, ddd, 15.2, 3.9 8.6, 3.9Hz), 1.52 (3H, d, 6.6Hz).

Please amend the paragraph at page 65, lines 7-14 to read as follows.

Major component: $^1\text{H-NMR}$ (CDCl_3) δ (ppm): 10.70 (1H, br), 9.02 (1H, br), 7.22 (1H, dd, 15.8, 11.2Hz), 6.61 - 6.65 (2H, m), 6.60 (1H, s), 6.53 (1H, m), 6.15 (1H, dd, 10.9, 10.6Hz), 5.89 - 5.98 (2H, m), 5.68 (1H, dd, 10.2, 3.0Hz), 5.47 (1H, m), 4.64 (1H, d, 15.5Hz), 4.61 (1H, br), 4.58 (1H, d, 16.2Hz), 4.06 (1H, br), 3.41 - 3.60 (2H, m), 3.54 (3H, s), 3.23 (1H, br), 3.00 (1H, m), 2.81 (2H, m), 2.34 (1H, ddd, 15.2, 3.3, 3.3Hz), 1.96 (1H, ddd, 16.2, 4.0 8.9, 4.0Hz), 1.55 (3H, d, 6.6Hz).

Please amend the paragraph starting at page 65, line 19 and ending at page 66, line 3 to read as follows.

¹H-NMR (CDCl₃) δ(ppm): 7.61 (1H, br), 7.16 (1H, dd, 16.0, 11.4Hz), 6.85 (2H, br), 6.60 (1H, d, 16.2Hz), 6.45 (1H, s), 5.79 (1H, dd, 11.2, 10.9Hz), 5.57 (1H, dd, 10.2, 3.0Hz), 5.43 (1H, m), 4.70 (1H, br), 4.67 (1H, d, 15.8Hz), 4.59 (1H, d, 15.8Hz), 3.95 (1H, br), 3.51 - 3.72 (2H, m), 3.15 (1H, br), 2.93 (1H, br d, 8.6Hz), 2.80 (2H, t, 5.6Hz), 2.72 (4H, br), 2.30 (1H, ddd, 14.9, 3.3, 3.3Hz), 1.98 (1H, ddd, 14.9, ~~4.3~~ 8.9, 4.0Hz), 1.52 (3H, d, 6.6Hz), 1.45 - 1.63 (6H, br).

Please amend the paragraph at page 66, lines 6-12 to read as follows.

¹H-NMR (CDCl₃) δ(ppm): 8.58 (1H, br), 7.05 (1H, dd, 16.2, 11.2Hz), 6.29 (1H, s), 5.98 (1H, d, 16.2Hz), 5.98 (1H, dd, 10.9, 9.2Hz), 5.55 (1H, br d, 10.2Hz), 5.45 (1H, m), 4.78 (1H, d, 15.8Hz), 4.68 (1H, d, 15.5Hz), 4.07 (2H, br), 3.98 (1H, br), 3.69 (1H, br), 2.84 - 3.04 (8H, m), 2.22 (1H, br d, 14.9Hz), 2.04 (1H, ddd, 14.5, ~~4.6~~ 10.4, 4.3Hz), 1.54 (3H, d, 6.9Hz), 1.20 - 1.48 (6H, br), 1.57 (3H, d, 6.9Hz).

Please amend the paragraph at page 67, lines 17-23 to read as follows.

Major component: ¹H-NMR (CDCl₃) δ(ppm): 10.76 (1H, br), 7.48 - 7.56 (2H, m), 7.25 - 7.37 (3H, m), 7.07 - 7.16 (2H, m), 6.77 (1H, d, 16.2Hz), 6.61 (1H, s), 6.21 (1H, dd, 11.6, 10.6Hz), 5.74 (1H, dd, 10.2, 3.6Hz), 5.52 (1H, m), 4.80 (1H, br), 4.73 (2H, s), 4.12 (1H, br), 3.23 (1H, br), 2.99 (1H, ddd, 8.3, 3.3, 2.6Hz), 2.36 (1H, ddd, 15.2, 3.6, 3.3Hz), 1.99 (1H, ddd, 15.2, ~~4.0~~ 8.6, 4.0Hz), 1.57 (3H, d, 6.9Hz).

Please amend the paragraph at page 68, lines 5-11 to read as follows.

Major component: ¹H-NMR (CDCl₃) δ(ppm): 8.00 (1H, br s), 7.43 (2H, d, 8.6Hz), 7.19 (2H, d, 8.3Hz), 7.20 (1H, m), 6.77 (1H, d, 16.2Hz), 6.59 (1H, s), 6.19 (1H, dd,

10.6, 9.9Hz), 5.73 (1H, dd, 10.2, 3.3Hz), 5.49 (1H, m), 4.72 (2H, s), 4.72 (1H, br), 4.09 (1H, br), 3.22 (1H, br), 2.82 - 3.01 (2H, m), 2.35 (1H, dd, 15.2, 3.3, 3.3Hz), 1.98 (1H, ddd, 15.2, ~~4.0~~ 8.6, 4.0Hz), 1.55 (3H, d, 6.6Hz), 1.22 (6H, d, 6.9Hz).

Please amend the paragraph at page 68, lines 16-23 to read as follows.

Major component: $^1\text{H-NMR}$ (CDCl_3) δ (ppm): 7.97 (1H, d, 9.2Hz), 7.38 - 7.44 (2H, m), 7.26 (1H, dd, 15.8, 11.5Hz), 6.81 - 6.86 (2H, m), 6.75 (1H, d, 16.2Hz), 6.56 (1H, s), 6.16 (1H, dd, 11.6, 10.2Hz), 5.69 (1H, dd, 10.6, 3.3Hz), 5.47 (1H, m), 4.73 (1H, d, 16.5Hz), 4.67 (1H, d, 14.9Hz), 4.64 (1H, br), 4.04 (1H, d, 14.5Hz), 3.75 (3H, s), 3.20 (1H, br), 2.96 (1H, ddd, 9.9, 3.6, 2.3Hz), 2.33 (1H, ddd, 15.2, 3.6, 3.3Hz), 1.94 (1H, ddd, 15.2, ~~4.0~~ 8.9, 4.0Hz), 1.53 (3H, d, 6.9Hz).

Please amend the paragraph at page 69, lines 5-12 to read as follows.

Major component: $^1\text{H-NMR}$ (CDCl_3) δ (ppm): 7.98 (1H, br s), 7.32 (2H, d, 8.9Hz), 7.29 (1H, m), 6.75 (1H, d, 16.2Hz), 6.64 (2H, d, 8.9Hz), 6.58 (1H, s), 6.18 (1H, dd, 11.9, 9.9Hz), 5.71 (1H, dd, 10.2, 3.0Hz), 5.48 (1H, m), 4.72 (1H, d, 16.8Hz), 4.71 (2H, s), 4.04 (1H, d, 15.8Hz), 3.31 (4H, q, 7.1Hz), 3.21 (1H, br), 2.99 (1H, ddd, 8.6, 2.6, 2.3Hz), 2.34 (1H, ddd, 15.2, 3.6, 3.3Hz), 1.96 (1H, ddd, 15.2, ~~4.0~~ 8.6, 4.0Hz), 1.55 (3H, d, 6.6Hz), 1.12 (6H, t, 7.1Hz).

Please amend the paragraph starting at page 69, line 17 and ending at page 70, line 2 to read as follows.

Major component: $^1\text{H-NMR}$ (CDCl_3) δ (ppm): 8.56 (1H, br d, 7.9Hz), 8.46 (1H, m), 8.30 - 8.34 (2H, m), 7.31 - 7.42 (2H, m), 6.76 (1H, d, 16.2Hz), 6.52 (1H, s), 6.17 (1H, dd, 10.9, 9.9Hz), 5.72 (1H, dd, 10.2, 3.0Hz), 5.48 (1H, m), 4.80 (1H, br), 4.77 (1H, d, 16.5Hz), 4.70 (1H, d, 16.5Hz), 4.03 (1H, d, 16.5Hz), 3.20 (1H, br), 2.95 (1H, m), 2.34 (1H, ddd, 15.2, 3.3, 3.3Hz), 1.97 (1H, ddd, 15.2, ~~4.3~~ 8.9, 4.0Hz), 1.56 (3H, d, 6.9Hz).

Please amend the paragraph at page 74, lines 17-24 to read as follows.

Major component: $^1\text{H-NMR}$ (CDCl_3) δ (ppm): 7.20 (1H, m), 6.77 (1H, d, 16.2Hz), 6.58 (1H, s), 6.16 (1H, dd, 11.6, 10.6Hz), 5.66 (1H, br d, 9.6Hz), 5.53 (1H, m), 4.77 (1H, br), 4.76 (1H, d, 16.5Hz), 4.69 (1H, 16.2Hz), 4.33 (2H, m), 4.00 (1H, br), 3.72 (2H, m), 3.64 - 3.65 (14H, m), 3.53 - 3.56 (2H, m), 3.37 (3H, s), 3.20 (1H, br), 2.98 (1H, br d, 8.6Hz), 2.34 (1H, ddd, 15.2, 3.6, 3.3Hz), 2.00 (1H, ddd, 15.5, ~~4.3~~ 8.6, 4.0Hz), 1.56 (3H, d, 6.6Hz).

Please amend the paragraph at page 75, lines 7-15 to read as follows.

Major component: $^1\text{H-NMR}$ (CDCl_3) δ (ppm): 10.80 (1H, br), 7.20 (1H, m), 6.77 (1H, d, 16.2Hz), 6.58 (1H, br), 6.58 (1H, s), 6.16 (1H, t, 10.9Hz), 5.67 (1H, br d, 9.9Hz), 5.51 (1H, m), 4.78 (1H, br), 4.76 (1H, d, 16.5Hz), 4.69 (1H, d, 16.5Hz), 4.31 - 4.35 (2H, m), 4.02 (1H, br), 3.73 (2H, t, 4.8Hz), 3.63 - 3.67 (6H, m), 3.54 - 3.57 (2H, m), 3.38 (3H, s), 3.19 (1H, br), 2.98 (1H, ddd, 9.2, 3.3, 3.3Hz), 2.34 (1H, ddd, 15.2, 3.6, 3.3Hz), 1.98 (1H, ddd, 18.8, ~~4.0~~ 8.9, 4.0Hz), 1.57 (3H, d, 6.9Hz).